SPOTLIGHT ON
MARYLAND

MHCC MARYLAND HEALTH CARE COMMISSION

PRESCRIPTION DRUG SPENDING IN MARYLAND

Which Therapeutic Classes Gained Share From 2004 to 2006?

In 2006, outpatient prescription drug spending in Maryland accounted for 15 percent of total health care spending.[1] While growth over the past few years has slowed from what it was in the late 1990s, there remains substantial activity—both increases and declines—within specific therapeutic domains. The introduction of blockbuster drugs, the expiration of patents, and related opportunities for substitution from brand to generic all have substantial impacts on the level of drug spending across therapeutic classes. Recent developments related to drug safety and efficacy have also led to the withdrawal of specific drugs from the market or restrictions on their use, in turn affecting the distribution of spending across therapeutic classes. This Spotlight examines those therapeutic drug classes with the largest growth in absolute share between 2004 and 2006 and some of the factors underlying those changes.

THERAPEUTIC CLASS AND SPENDING SHARE GROWTH The share of drug spending for each therapeutic class was calculated for 2004 and 2006 and the classes were ranked by the absolute growth in the share. The top 10 fastest growing therapeutic classes in terms of spending share are shown in Table 1. Together, these 10 classes accounted for just under 15 percent—$183 million—of total drug spending for privately insured Maryland residents under 65 years of age in 2006.[2,3] The 2006 share of spending for each of these drug classes appears to be relatively modest, ranging from 0.8 percent to 2.4 percent of total prescription drug spending. (In fact, spending is fairly evenly distributed across classes—three-quarters of the 131 drug classes have spending shares of less than 1 percent and only 8 have shares of more than 3 percent.) In terms of absolute growth in spending share between 2004 and 2006, the largest increase is 0.8 percent for antihyperlipidemic combinations, followed by 0.5 percent for miscellaneous anxiolytics, sedatives, and hypnotics, and for antihypertensive combinations. Below we explore some of the factors underlying share growth.

ABSOLUTE GROWTH IN SPENDING SHARE VS. GROWTH IN SPENDING Spending share is the proportion of overall prescription drug spending attributable to a specific therapeutic class. The absolute growth is calculated by subtracting the share in 2004 from the share in 2006. Classes of drugs that saw increases in spending share grew faster than overall spending. Many drug classes experienced spending growth but their share of spending did not increase. Loss of absolute share does not indicate that growth in spending was negative.

THERAPEUTIC CLASS Group of pharmaceutical agents that are chemically or therapeutically related. A grouping devised for the Multum Lexicon database from Cerner Multum, Inc., was used, which relies on 131 therapeutic classes.

SPENDING PER MEDICATED DAY Amount paid for a given prescription (including both insurer and patient portions), divided by the number of days supplied.

DRUG PRICE INFLATION As a factor accounting for drug spending growth, increases in drug prices played a somewhat smaller though still prominent role in 2006, accounting for approximately half of overall growth, while expansions in use and other elements not related to price are making an increasing contribution over time.[4] In selected market segments, substitution of generics has been one source of downward pressure on overall drug price growth. Where patents remain in place, however, and there are few generic substitutes, price increases have been more common. In this Spotlight, we examine mean spending per medicated day in order to isolate changes in price for a given set of drugs from changes in the number of users.[5]

TABLE 1. Fastest Growing Therapeutic Classes, Ranked by Absolute Share Growth, 2004–2006

THERAPEUTIC MINOR AND (MAJOR) DRUG CLASS	DESCRIPTION AND USES OF DRUGS IN CLASS	ABSOLUTE SHARE GROWTH, 2004–2006	SHARE OF TOTAL SPENDING, 2006
ANTIHYPERLIPIDEMIC COMBINATIONS (Antihyperlipidemic agents)	Composed of a combination of chemicals that lower LDL, raise HDL, and lower total cholesterol and triglycerides.	0.80%	0.88%
MISCELLANEOUS ANXIOLYTICS, SEDATIVES, AND HYPNOTICS (Central nervous system agents)	Induce sleep by depressing the central nervous system and/or reducing electrical activity in the brain to treat symptoms of anxiety and promote relaxation.	0.54	1.53
ANTIHYPERTENSIVE COMBINATIONS (Cardiovascular agents)	Composed of a combination of chemicals that prevent constricting of blood vessels and increase the amount of salt and water lost through urine (i.e., diuretics). Used together to lower blood pressure.	0.53	2.40
ANTIVIRAL COMBINATIONS (Anti-infectives)	Kill or prevent the growth of viruses, such as HIV and hepatitis.	0.48	1.05
MONOCLONAL ANTIBODIES (Immunologic agents)	Most widely used form of cancer immunotherapy at this time; also used to treat allergy-related asthma and certain autoimmune disorders, including rheumatoid arthritis, psoriasis, and Crohn's Disease.	0.42	0.79
ANTIRHEUMATICS (Miscellaneous agents)	Suppress the inflammatory process and help decrease the pain and swelling found in a variety of autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosis, and psoriatic arthritis.	0.42	1.53
THIAZOLIDINEDIONES (Hormones)	Antidiabetic agents used as adjunctive therapy to help reduce the insulin resistance that is characteristic of Type II diabetes.	0.31	1.73
INSULIN (Hormones)	A naturally occurring hormone used to treat both Type I (insulin deficiency) and Type II (insulin resistance) diabetes.	0.30	1.46
SSNRI ANTIDEPRESSANTS (Psychotherapeutic agents)	Prescribed for the treatment of anxiety and clinical depression disorders.	0.29	1.99
LEUKOTRIENE MODIFIERS (Respiratory agents)	Treat asthma by blocking the body's production or use of leukotrienes, thereby preventing or lessening inflammation and helping to keep airways open.	0.25	1.41

Table 2 shows mean spending per medicated day in 2006 as well as the annualized growth in that spending from 2004 to 2006, in order to better understand sources of growth within the therapeutic classes. In 4 of the 10 therapeutic classes, annualized growth in daily spending was substantial and likely a driving force behind the share growth in those drug categories. For miscellaneous anxiolytics, sedatives, and hypnotics and antihypertensive combinations, daily spending grew at an average annual rate of 13.8 percent and 12 percent, respectively. For antirheumatics and insulin, annualized spending per medicated day was somewhat more rapid, increasing 18 percent and 16.4 percent, respectively. Spending growth in the class of miscellaneous anxiolytics, sedatives, and hypnotics was fueled in part by direct-to-consumer advertising and higher-than-average price increases for Ambien®, which holds about two-thirds of the market for hypnotics.[6]

INCREASES IN THE PREVALENCE OF USE As drug prices have become less of a factor in recent drug spending growth, the role of increased use has risen. This growth in volume has been attributed to a number of factors, including the increased access to prescription drugs afforded by the implementation of the Medicare drug benefit as well as the availability of less expensive generic alternatives, heightened demand for pharmaceuticals precipitated in part by direct-to-consumer advertising, and the continually expanding therapeutic reach of pharmaceuticals.

For 6 of the 10 therapeutic classes, annualized growth in the number of users was substantial and likely a major factor in the share growth for those categories. For antihyperlipidemics, the rise in volume was dramatic—56 percent annually. In addition to FDA approval of a new combination treatment in this drug class (discussed below), factors that may have played a role in expanding demand in this therapeutic area were continuing high rates of cardiovascular disease and expanding screening and treatment efforts as well as high levels of direct-to-consumer advertising.[7] Two other therapeutic classes—antiviral combinations and monoclonal antibodies—experienced average annual user growth of over 20 percent, while for 3 other drug categories the annualized increase was over 10 percent.

NEW DRUG APPROVALS AND BRAND-GENERIC TRENDS A major factor contributing to share growth appears to be the introduction of new drugs within these therapeutic categories. Three of the 4 top-ranked drug classes include at least two new drug approvals between 2004 and 2006. For miscellaneous anxiolytics, hypnotics, and sedatives, there were two new patents in 2005 and one in 2004; however, in 2006 the newer drugs, including Ambien CR®—an extended release formulation[8]— still accounted for a relatively small portion of the overall market for sleep medications. With the expiration of the patent on Ambien® in 2007, it is not clear how the status of Ambien CR® will counteract that potential market share loss. For antiviral combinations, there were new patents in both 2004 and 2006; one of these, Atripla®, is a new once-daily combination medication. Neither of these two classes (miscellaneous anxiolytics or antivirals) had any patent expirations.

For antihypertensive combinations, FDA approvals for new drugs were obtained in 2006, 2004, and 2003; insulin also included multiple approvals, two in 2006 and 2005. In the remaining 5 classes, 1 includes a 2004 approval, 1 had a new drug introduced in 2003, and the others had additions in 1998–2002. Much of the increase for antihypertensive combinations is related to use of two drugs gaining approval in and around that time period (Caduet®, a combination calcium channel blocker and statin, and Benicar HCT®, a combination angiotensin II receptor blocker and diuretic). The drug Cymbalta®, used to treat depression and also nerve pain in diabetics, is responsible for the growth in SSNRI antidepressants, while the increase in share for antirheumatics is almost exclusively due to Enbrel®, a biologic used to treat immune and inflammatory disorders such as rheumatoid arthritis and psoriasis. In the insulin or antidiabetic drug class, there were a number of new approvals, including the first-ever inhaled form of insulin, Exubera®. Other long-acting insulins were approved during the period as well.

Not surprisingly, generic spending is much lower in those classes where spending share growth is higher: in the 25 therapeutic classes with the highest share growth, the average generic spending per class is less than 5 percent compared to almost 40 percent average spending on generics in the 25 classes with the lowest share growth.[9] And, in fact, for the top 10 therapeutic classes, there was very little generic penetration. For 6 of the classes there is no generic availability at all, and for 1 of the categories spending on generics is less than 1 percent (see Table 2). Only 1 of the 10 therapeutic categories—antihypertensive combinations—has generic spending above 10 percent.

TABLE 2. Selected Descriptive Statistics on Fastest Growing Therapeutic Classes

THERAPEUTIC DRUG CLASS	TOTAL SPENDING, 2006* ($MILLIONS)	ANNUALIZED GROWTH IN TOTAL SPENDING, 2004–2006	MEAN SPENDING PER MEDICATED DAY, 2006	ANNUALIZED GROWTH IN SPENDING PER MEDICATED DAY, 2004–2006	TOTAL NUMBER OF USERS, 2006	ANNUALIZED GROWTH IN NUMBER OF USERS, 2004–2006	MAJOR NEW DRUG APPROVALS**	PERCENT SPENDING ON GENERICS, 2006
ANTIHYPERLIPIDEMIC COMBINATIONS	$10.9	312.3%	$2.77	4.3%	21,712	56.2%	Vytorin®, 07/2004	0.0%
MISCELLANEOUS ANXIOLYTICS, SEDATIVES, AND HYPNOTICS	19.1	34.1	2.98	13.8	75,455	8.9	Rozerem®, 07/2005 Ambien CR®, 09/2005 Lunesta®, 12/2004	7.0
ANTIHYPERTENSIVE COMBINATIONS	29.9	21.9	1.35	12.0	98,455	6.4	Dutoprol®, 08/2006 Caduet®, 01/2004 Benicar HCT®, 6/2003 Diovan HCT®, 03/1998	12.0
ANTIVIRAL COMBINATIONS	13.0	46.5	26.27	6.2	2,490	21.3	Atripla®, 06/2006 Truvada®, 08/2004 Epzicom®, 08/2004	0.0
MONOCLONAL ANTIBODIES	9.9	57.4	54.96	5.8	1,027	28.2	Xolair®, 06/2003 Humira®, 12/2002	0.0
ANTIRHEUMATICS	19.0	27.5	15.87	18.0	6,037	6.5	Enbrel®, 11/1998	4.4
THIAZOLIDINEDIONES	21.5	19.2	4.59	4.5	22,180	10.6	Avandia®, 05/1999	0.0
INSULIN	18.1	20.8	4.08	16.4	19,173	3.2	Exubera®, 01/2006 Levemir®, 09/2005 Lantus®, 04/2000 Novolog®, 06/2000	0.0
SSNRI ANTIDEPRESSANTS	24.7	16.5	4.47	1.2	30,905	11.4	Cymbalta®, 08/2004	0.7
LEUKOTRIENE MODIFIERS	17.5	18.8	3.09	5.4	40,427	12.6	Singulair®, 02/2002	0.0

* Due to rounding, total drug spending in Maryland in 2006 appears higher in Table 2 than is reported on page 1 of the Spotlight.

** Drugs listed under "Major New Drug Approvals" are drugs recently approved by the FDA during or shortly prior to the study period, or drugs with no therapeutic equivalents, that contributed substantially to increased drug spending within the corresponding therapeutic drug class from 2004 to 2006.

While there were a large number of drug approvals in the period examined, there were also a large number of patent expirations in 2006. Many of the expirations have been in these top-ranked therapeutic classes, with the impact likely to be seen in increased generic substitution in the future leading to continued moderate price growth. In the case of antihyperlipidemics, 2006 witnessed generic availability for Pravachol® and Zocor®. Other generic introductions included versions of two antidepressants—Zoloft® and Wellbutrin XL®. And, as mentioned earlier, Ambien® lost its patent protection in 2007, though its extended release formulation remains under patent.

THERAPEUTIC CLASSES WITH DECLINING SHARE (DATA NOT SHOWN) As the share of spending for the therapeutic drug classes discussed above has outpaced all other therapeutic classes, it follows that some classes have experienced substantial declines in their share of spending over the same time period. Many of the therapeutic classes with the most significant declines in spending share fell into the same major drug classes as those discussed above with increasing share. In other words, there was frequently a direct offset with declines in one formulation attributable to growth in another within a broad drug grouping.

Often the offset was due to the development of combination drugs. In one such case, the share of spending attributable to HMG-CoA reductase inhibitors fell by 0.6 percent, a decline only slightly smaller than the rise in share for antihyperlipidemic combinations, both of which belong to the major drug class of antihyperlipidemic agents. Similarly, among cardiovascular agents, the absolute share growth for angiotensin converting enzyme (ACE) inhibitors and calcium channel blocking agents—both prescribed for the treatment of hypertension—decreased by about 0.3 percent each while the spending share of their newer counterparts, antihypertensive combinations, rose by 0.5 percent. The spending share for NRTIs—older, monotherapeutic anti-HIV drugs within the grouping antiviral agents—also fell while that for antiviral combinations increased.

Other share declines occurred for different reasons. Within the major drug class of psychotherapeutic agents, the share of spending on SSRI antidepressants fell, likely related to FDA advisories beginning as early as 2004 warning about potentially adverse outcomes in children, and resulting in at least some patients' switching from the older SSRI antidepressants to the newer—and more expensive—SSNRIs. SSRIs still maintained a relatively large spending share of almost 4 percent in 2006, though the share drop in the two prior years was substantial. Likewise, the share of spending for COX-2 inhibitors fell by just over 1 percent when the drugs experienced a substantial drop in the number of users, not surprising given evidence that several of the most widely used of these drugs are associated with increased risk of cardiovascular events. A mild cold and flu season may have contributed to the share decline for macrolides and quinolines, both therapeutic classes within the broader grouping of anti-infectives, which saw drops of 0.4 percent and 0.3 percent in share, respectively. Macrolides also saw a substantial drop in spending with a generic introduction for Zithromax®.

COMING TRENDS This Spotlight has focused on those therapeutic drug classes that have experienced the largest absolute growth in share between 2004 and 2006. While there is substantial overlap with those therapeutic categories that have the highest dollar volume overall or had the highest growth in spending, these are not necessarily the same categories. Several of the therapeutic categories discussed here—for example, monoclonal antibodies and antihyperlipidemic combinations—have smaller market shares when compared to other therapeutic classes—such as gastrointestinals or antiasthmatics—that are much larger measured in dollar value but may not have experienced a growth surge during the period examined.

It is clear from the drug approvals noted in Table 2 that there is a growing use of combination drugs in which two or more medications are combined and administered in a single dose (note that 3 of the 10 therapeutic classes are themselves "combinations"). This trend seems to be driven at least in part by declining sales or impending patent expirations; in addition, manufacturers argue that patients will be more compliant if they have fewer prescriptions to fill, co-pays to make, and pills to take.

In general, spending growth is likely to be moderate in the near future. While there are a number of drug approvals anticipated in the next few years, few are expected to have large impacts on the drug spending trend. Trend projections can be problematic, especially given unexpected evidence from clinical trials or other large research studies that can often dramatically redirect drug spending.[10] However, while

blockbuster drugs may not be pushing prices upward, there will also be only a small number of new generic drugs available after 2009 that are expected to have large downward impacts on use and cost trends. There are two exceptions worth noting. With respect to drug approvals, an exception may be for the therapeutic class of antidiabetics, where four new drugs received approval in 2006. Growth in this therapeutic area may also be driven by increases in the incidence of obesity—a risk factor for Type II diabetes—among both children and adults. In terms of generics, the exception is a generic Lipitor that will become available in 2010.

While spending growth over the next few years will remain moderate, prescription spending growth is expected to rise over time reaching an annual growth rate of almost 10 percent by 2016.[11] Much will depend on the level of innovation within the pharmaceutical industry. In particular, continued developments within specialty pharmacy—high-cost medications that often require special handling and administration and usually rely on recombinant technology and processes—may have a substantial impact on overall cost trends, though specialty medications are currently used by a small proportion of the population.[12] Continued spending growth will call for an active role for pharmacy benefits management. PBMs are increasingly relying on multiple strategies with emphasis on generic dispensing at the core of cost containment.

[1] Maryland Health Care Commission, State Health Care Expenditures: Experience from 2006, Released January 2008.

[2] Tables in this report are based on services and payments captured in the Prescription Drug Component of the Medical Care Data Base (MCDB), which includes insurance claim records of noninstitutional and professional services rendered by physicians and nonphysician health care professionals to patients who live in Maryland. The Prescription Drug Component is based on a subset of data found on insurance claims paid by most private insurers in Maryland. Insurance companies and HMOs meeting certain criteria, namely, that they are licensed in Maryland and collect more than $1 million in health insurance premiums, are required to submit information to MHCC under the Code of Maryland Regulations (COMAR) 10.25.06. Estimates are limited to persons covered by drug contracts with large Maryland insurers (e.g., if an employer, such as the State of Maryland, contracts directly with a pharmacy benefit manager for drug coverage, then use is not included). The data include both retail store and mail order prescription spending.

[3] Differences in total drug spending in Maryland in 2006 on page 1 of this Spotlight and in Table 2 are due to rounding.

[4] A Catlin, C Cowan, M Hartman, S Heffler, and the National Health Expenditure Accounts Team, National Health Spending In 2006: A Year Of Change For Prescription Drugs, *Health Affairs*, January/February 2008.

[5] Note that this does not account for changes in dosage or formulation.

[6] A study by AARP found that price increases for Ambien® (5 mg and 10 mg) were among the highest for brand-name drug products in the first nine months of 2006; it should be noted that manufacturer price changes are not necessarily passed on in their entirety to consumers. In addition, different dosages of Ambien® and other drugs were studied. It is likely that the price increases were for Ambien CR®, which obtained FDA approval in 2005. The study can be accessed at http://assets.aarp.org/rgcenter/health/dd151_drugprices.pdf. See also Express Scripts 2006 Drug Trends Report, page 27, which notes that direct-to-consumer advertising was higher for hypnotics than for any other class in 2006. Data tabulations from the Prescription Drug Component of the MCDB used for this Spotlight indicate that in 2006 spending for Ambien® (zolpidem) accounted for $13.2 million of total drug class spending of $19 million, or 69 percent. This includes spending on Ambien® and Ambien CR®.

[7] Express Scripts 2006 Drug Trends Report.

[8] Sanofi Aventis responded to the expiration of the patent on Ambien® by introducing a long-acting formulation Ambien CR® in 2006.

[9] These calculations are from the Prescription Drug Component of the MCDB. According to the Generic Pharmaceutical Association, the generic dispensing rate reached 63 percent in 2006.

[10] Recent evidence about Vytorin®—indicating that although it reduces major risk factors, it does not have a significant effect on heart disease—is likely to have an adverse impact on Vytorin® sales, though it is too early to assess the extent of the impact on drug spending. Kastelein JJ, Akdim F, Stroes ES, Zwinderman AH, Bots ML, Stalenhoef AF, Visseren FL, Sijbrands EJ, Trip MD, Stein EA, Gaudet D, Duivenvoorden R, Veltri EP, Marais AD, de Groot E; the ENHANCE Investigators. Simvastatin with or without Ezetimibe in Familial Hypercholesterolemia. *New England Journal of Medicine*. 3 April 2008; 358(14): pp1431-1443.

[11] JA Poisal, C Truffer, et al, and the National Health Expenditure Accounts Team. Health Spending Projections Through 2016: Modest Changes Obscure Part D's Impact. *Health Affairs*. 2007; vol 26: pp242-253.

[12] They are often used to treat complex or rare conditions such as rheumatoid arthritis, multiple sclerosis, blood cell deficiencies, and respiratory disorders; the number of users is quite small, perhaps less than 3 percent of the population. However, specialty medications had a large impact on spending trends in 2006 and certainly will in the years to follow. The Walgreens Health Initiatives Outlook Trends Report 2007 reported that the average cost per prescription for a specialty medication was $1,575 in 2006, approximately 21 times more than the average cost for a nonspecialty medication. Moreover, the report indicated that costs for specialty medications are expected to grow about twice as fast as costs for nonspecialty medications.

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